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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,037	09/17/2003	Richard D. Guarino	P-6186	2610

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EXAMINER	
AFREMOVA, VERA	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 10/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/664,037	GUARINO ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-16 and 58-67* is/are pending in the application.

4a) Of the above claim(s) *9,11,59 and 60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 6-8, 10, 12-16, 58, 61-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: translation of EP 0432265?

DETAILED ACTION

Claims 1-3, 6-8, 10, 12-16, 58 and 61 as amended and new claims 62-67 are under examination in the instant office action.

Claims 9, 11, 59 and 60 were withdrawn from further consideration pursuant to 37 CFR 1.142(b), as drawn to combination of nonelected species without traverse (12/21/2005).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 1-4, 7, 8 and 12-15 as amended and new claims 62-64 remain/are rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/56897 as explained in the prior office action.

Claims are directed to a method for culturing liver cells wherein the method comprising (a) providing a polymer composition comprising a cell adhesion resistant (CAR) material, ECM protein(s) and a polycationic polymer in order to form a cell adhesion promoting surface; and (b) incubating the liver cells in the presence of the surface and a culture medium wherein the liver cells attach to the surface and are maintained in a functional state. Some clams are further dawn to the use the ECM proteins such as collagen type I and to the CAR material such as hyaluronic

acid (HA). Some claims are further drawn to the use of 3D scaffold formed by ECM proteins and to the use of flexible material in the surface polymer composition.

WO 98/56897 discloses a method for attaching and maintaining primary porcine liver cells in a functional state (page 13, example 6) by incubating the liver cells in a culture medium on a nonwoven HYAFF in co-culture with dermal fibroblasts that are seeded on the nonwoven HYAFF. The HYAFF matrices are made from hyaluronic acid (paragraph bridging pages 1 and 2). ECM proteins including collagen type I are provided by dermal fibroblasts. The dermal fibroblast ECM proteins provide for 3D scaffold for liver cells. The liver cell culture is maintained in plastic 24-well dishes that are made from plastic or generic flexible material within the broadest meaning of the claims. Plastic is polymer or a generic polycationic polymer within the broadest meaning of the claim. The liver cells are maintained alive for several weeks (page 13) and, thus, they are in functional state including p450 activity and ability to secrete albumin that are inherent features of hepatocytes. Thus, the cited method comprises identical active steps and identical structural elements as required by the claimed method. Therefore, the cited reference anticipates the claimed invention.

2. Claims 1-3, 7, 8, 14-16 as amended and new claims 62-64 remain/are rejected under 35 U.S.C. 102(e) as being anticipated by US 6,562,616 (Toner et al) as explained in the prior office action.

Claims are directed to a method for culturing liver cells wherein the method comprising (a) providing a polymer composition comprising a cell adhesion resistant (CAR) material, ECM protein(s) and a polycationic polymer in order to form a cell adhesion promoting surface; and (b)

incubating the liver cells in the presence of the surface and a culture medium wherein the liver cells attach to the surface and are maintained in a functional state. Some clams are further dawn to the use the ECM proteins such as collagen type I. Some claims are further drawn to the use of 3D scaffold formed by ECM proteins and to the use of flexible material in the surface polymer composition such as PDMS.

US 6,562,616 (Toner et al) discloses a method for attaching and/or maintaining primary porcine liver cells (col. 24, lines 52-63) wherein the method comprising incubating the liver cells on collagen type I coated glass slides (generic CAR material). The ECM proteins such as collagen type I provide liver cells for 3D scaffold within the meaning of the claims. US 6,562,616 also teaches the use of a polycationic polymer or PDMS polymer materials for forming the surface composition in the method for culturing liver cells. The liver cells are maintained in viable state (example 8) and, thus, they are in functional state including p450 activity and ability to secrete albumin that are inherent features of hepatocytes. Therefore, the cited method comprises identical active steps and identical structural elements as required by the claimed method. Therefore, the cited reference anticipates the claimed invention.

3. Claims 1-3, 7, 8, 14, 15 and 61 as amended and new claims 62-64 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,942,436 (Dunn et al) as explained in the prior office action.

Claims are directed to a method for culturing liver cells wherein the method comprising (a) providing a polymer composition comprising a cell adhesion resistant (CAR) material, ECM protein(s) and a polycationic polymer in order to form a cell adhesion promoting surface; and (b)

incubating the liver cells in the presence of the surface and a culture medium wherein the liver cells attach to the surface and are maintained in a functional state. Some clams are further dawn to the use the ECM proteins such as collagen type I. Some claims are further drawn to the use of 3D scaffold formed by ECM proteins and to the use of flexible material in the surface composition. Some claims are further drawn to the use of rat liver cells.

US 5,942,436 (Dunn et al) discloses a method for culturing primary liver cells such as rat hepatocytes (col. 5, line 38) and human hepatocytes (col. 8) in culture vessels coated with collagen type I (rat tail collagen) (col.6, lines 5-26). The liver cell culture is maintained in a generic plastic dish that is made from plastic or generic flexible material within the broadest meaning of the claims. Plastic is polymer that is a generic CAR material and a generic polycationic polymer within the broadest meaning of the claims. The patent teaches that liver cells are maintained in functional state as suitable for replacing liver function in vivo (col.8, lines 19-25) and thus, they have p450 activity and ability to secrete albumin that are inherent features of functional hepatocytes.

Thus, the cited method comprises identical active steps and identical structural elements as required by the claimed method. Therefore, the cited reference anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 6-8, 10, 12-16, 58 and 61 as amended and new claims 62-67 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/56897, US 6,562,616 (Toner et al) and US 5,942,436 (Dunn et al) taken with US 6,653,105 (Triglia et al) and JP 04322657 as explained in the prior office action.

The cited WO 98/56897, US 6,562,616 (Toner et al) and US 5,942,436 (Dunn et al) teach methods for culturing mammalian liver cells including rat and human liver cells attached to ECM proteins such as collagen type I that is coating or bound to non-adhesive (CAR) materials including HA. The cited references are lacking particular disclosure about the use of poly-L-ornithine in the surface coating composition in the method for culturing liver cells.

However, US 6,653,105 (Triglia et al) teaches methods for culturing mammalian liver cells including human hepatocytes (col. 4, line 6) and suggests the use of attachment surfaces that are composed of poly-ornithine and collagen as suitable compositions for attachment, incubating and growing hepatocytes (col. 6, lines 5-24).

In addition, the cited JP 04322657 also teaches and/or suggests culturing liver cells in the presence of biologically active composition such as a mixture of materials selected from collagen, poly-L-ornithine, glasses, organic polymers and/or silicone-based rubbers (English abstract).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to add poly-L-ornithine to the coating polymer compositions of WO 98/56897, US 6,562,616 (Toner et al) and/or US 5,942,436 (Dunn et al) with a reasonable expectation of success in culturing liver cells because the cell attachment surfaces comprising

poly-L-ornithine and collagen type I have been taught and/or suggested by the prior art of attaching, incubating and growing hepatocytes as adequately demonstrated by the cited reference combined. The cited references are in the same field of endeavor and seek to solve the same problems as the instant application and claims, and one of skill in the art is free to select components available in the prior art, *In re* Winslow, 151 USPQ 48 (CCPA, 1966).

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicant's arguments filed 7/17/2006 have been fully considered but they are not persuasive.

With regard to the claim rejection under 35 U.S.C. 102(b) as being anticipated by WO 98/56897, US 6,562,616 (Toner et al) or US 5,942,436 (Dunn et al) applicants argue that the disclosed methods of culturing liver cells do not comprise the use "a polycationic polymer" in the materials of the culture vessel. However, the culture vessels are made from generic plastic materials that are generic polycationic polymers within the broadest meaning of the claims.

With regard to the claim rejection under 35 USC § 103 applicants argue that the cited WO 98/56897, US 6,562,616 (Toner et al) and/or US 5,942,436 (Dunn et al) are silent about the use of polyornithine as "polycationic polymer" in the materials of the culture vessel and that the cited secondary references US 6,653,105 (Triglia et al) and JP 04322657 teach the use of

polyornithine as an invitation for experimentation rather than a direct suggestion. This argument is not found persuasive because US 6,653,105 (Triglia et al) and JP 04322657 clearly teach the use of polyornithine and collagen in the list of materials suitable for attachment and maintenance of liver cells. The cited references are in the same field of endeavor and seek to solve the same problems as the instant application and claims, and one of skill in the art is free to select components available in the prior art, *In re* Winslow, 151 USPQ 48 (CCPA, 1966).

Moreover, motivation can come not only from direct teaching of the prior art, but also the nature of the problem to be solved and/or the knowledge of persons of ordinary skill in the art, Ruiz v. A.B. Chance Co. 357 F.3d 1270, 69 USPQ2d 1686 (2004). The cited references are in the same field of endeavor and seek to solve the same problems as the instant application and claims, and one of skill in the art is free to select components available in the prior art, *In re* Winslow, 151 USPQ 48 (CCPA, 1966). Further, the examiner recognizes that references cannot be arbitrarily combined that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references, *In re* Nomiya, 184 USPQ 607 (CCPA 1975). However, there is no requirement that a motivation to make the modification be expressly articulated. One test for combining references is what the combination of disclosures taken as a whole would suggest to one versed in the art, rather than by their specific disclosures, *In re* Bozek, 163 USPQ 545 (CCPA 1969).

In this case, all particular claimed components including HA, collagen type I and poly-L-ornithine are known in the art, and used for their known art specific properties, in different combination for culturing liver cells as adequately demonstrated by the cited references. Thus,

the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

September 28, 2006

VERA AFREMOVA

PRIMARY EXAMINER